REMARKS

This is in response to the Official Action of September 7, 2001. Reconsideration in light of the amendments herein and the remarks below is respectfully requested.

Claims 1-12 and 14-28 stand rejected under the first paragraph of 35 USC 112 as lacking enablement. Reconsideration for the reasons set forth below is respectfully requested.

First, the claims have been reviewed in light of *Enzon Biochem Inc. v. Calgene Inc.*, 188F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999). In *Enzon*, certain claims concerning antisense technology were held invalid as lacking enablement. The court particularly noted (a) the unpredictability of the technology, (b) the breadth of the claims extending from E. coli to a variety of prokaryotic and eukaryotic cells such as tomato, and (c) the failure of examples within the scope of the claims.

The patents in dispute in *Enzon* had a priority date of 1983. The instant application has a priority date of 1997. It is well settled that enablement is evaluated as of the filing date of the patent or application in issue. Here, antisense technology has evolved considerably since 1983, to the point that it is considered to provide a rational basis for drug design. In fact, a search of the USPTO patent database using the phrase "aclm/antisense" reveals over 1,000 issued United States patents that utilize the feature "antisense" in the claims. All must be presumed to be valid by operation of law. Hence, the present application does not concern an unpredictable field.

In *Enzon*, there was considerable concern with the vast variety of species encompassed, extending from procaryotes to eukaryotes and from microorganisms to vascular plants. In the instant case there is no such scope, as the invention is concerned with the treatment of mammalian subjects. To clarify this point the claims have been amended to recite "mammalian", support for which is found in the specification at page 16 line 7.

Finally, in *Enzon* the court was concerned with failed experiments attempting to carry out the invention which had been conducted under the direction of the invention. Here there are no such failed experiments.

Accordingly, it is respectfully submitted that this invention satisifes the criteria of enablement as stated and applied in *Enzon*, and respectfully submitted that this rejection should be withdrawn.

Second, applicants respectfully disagree with the Examiner's analysis of the Rule 132 evidence submitted by the applicants. The use of *in vitro* models such as utilized by applicant for satisfying the enablement requirement is expressly approved by the CAFC in *In re Brana,* 51 F.3d. 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). Further, as previously discussed, the **Bentires-Alj** reference relied upon by the Examiner utilizes stably transformed cell lines which are outside the scope of the instant claims. The instant invention uses exogenous administration of the the NF-kb inhibitor, such as by administration of a viral vector. The claims have been further amended to recite "transiently administering", the only type of administration with which applicant is concerned, to better distinguish this point.

In view of the above, Applicants submit that the present application is in condition for allowance, which action is respectfully requested.

The changes made to the claims herein are shown, with additions underlined and deletions bracketed, in the attached "Version with Markings to Show Changes Made".

Respectfully submitted,

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PATENT TRADEMARK OFFICE

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, DC 20231, on 7 March 2002.

Vickie Diane Prior
Date of Signature: 7 March 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (twice amended) A method of enhancing the cytotoxic effects of an antineoplastic chemotherapeutic agent, comprising transiently administering to a mammalian subject in need of such therapy a therapeutically effective amount of an NF-κB inhibitor in conjunction with the administration of the chemotherapeutic agent, whereby the cytotoxic effect of said chemotherapeutic agent is increased compared to that which would occur in the absence of said NF-κB inhibitor.

6. (twice amended) A method of enhancing chemotherapeutic cytotoxicity in a mammalian subject treated with an antineoplastic chemotherapeutic agent, comprising transiently administering to the mammalian subject a therapeutically effective amount of an NF-κB inhibitor in conjunction with the administration of the chemotherapeutic agent, whereby the cytotoxic effect of said chemotherapeutic agent is increased compared to that which would occur in the absence of said NF-κB inhibitor.

11. (twice amended) A method of enhancing chemotherapeutic cytotoxicity in a mammalian subject treated with intratumoral TNFα, comprising transiently administering to the mammalian subject a therapeutically effective amount of NF-κB inhibitor in conjunction with the administration of TNFα, whereby the cytotoxic effect of said TNFα is increased compared to that which would occur in the absence of NF-κB inhibitor.

14. (amended) A method of treating a tumor in a mammalian subject with a chemotherapeutic agent, the improvement comprising transiently administering an effective amount of an NF-κB inhibitor in conjunction with said chemotherapeutic agent, whereby the cytotoxic effect of said chemotherapeutic agent is increased compared to that which would occur in the absence of said NF-κB inhibitor.

15. (amended) A method of treating a mammalian subject receiving a chemotherapeutic agent for the treatment of a neoplastic growth, the improvement comprising transiently administering an effective amount of an NF-κB inhibitor to the subject in conjunction with said chemotherapeutic agent, wherein the effect is to increase the cytotoxic effects of said chemotherapeutic agent.

16. (amended) A method of increasing the cytotoxicity of a chemotherapeutic drug administered to a mammalian subject for the treatment of a neoplastic growth, comprising transiently administering an effective amount of an NF-κB inhibitor to said subject in conjunction with said chemotherapeutic drug, wherein the effect is to increase the cytotoxic effects of said chemotherapeutic drug.

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